

## **REMARKS**

### ***Introduction***

Claims 1-13 and 18-24 are currently pending in the application, claims 14-17 and 25-42 have been cancelled. Only claim 1 is in independent form.

### ***Claim Rejections - 35 USC 103***

Claims 1-13 and 18-24 have been rejected under 35 U.S.C. 103(a) as being unpatentable over Muffler (DE 2823969) in view of Regan (U.S. Patent 3,683,092).

Applicant notes the following arguments used by the Examiner in the Final Rejection.

“Such reactants differ only as to substituents that are removed from the reaction site and do not enter into the reaction. One would not expect the different substituents to affect the outcome of the reaction.”

“Electronic and steric factors of the fluorinated methyl groups would not have been expected to affect the outcome of the reaction. First, the reaction takes place at the chloro- group which is removed from the fluorinated methyl groups of the  $(CF_3)_2CHOCH_2Cl$  reactant.”

“One would not expect the electronic and steric factors of the fluorinated methyl groups so removed to greatly influence the outcome of the reaction.”

Applicant respectfully submits that the Examiner's arguments above about what one of skill in the art would expect are based upon hindsight, and that even structurally similar reactants often do not follow recognized theoretical principles.

The Examiner asserts, among other things, that the fluorination of sevochlorane with amine hydrofluorides to give sevoflurane is obvious. The reasoning seems to be that (1) the Muffler starting material has structural similarities to sevochlorane, and (2) the other Muffler

reactants (the amine hydrofluoride) are the same as those in the present claims, and therefore one of skill in the art would recognize that fluorination at the primary carbon off the oxygen would occur with sevochlorane.

However, the fluorination of chloroethers is not predictable simply from knowing that the chloroether to be fluorinated is similar in structure to one having known susceptibility to a given fluorination agent. There are experimental data available for the case at hand relative to whether or not the reaction of  $(CF_3)_2CHOCH_2Cl$  could accurately be predicted from the prior art. It would appear reasonable to suggest, based on Muffler and Regan, that the reaction of  $(CF_3)_2CHOCH_2Cl$  with amine hydrofluorides be tried. However, it does not appear reasonable to predict with certainty that the reaction would work. There is ample precedent in the law that a mere suggestion to try is not enough to render claims unpatentable. *Uniroyal, Inc. v. Rudkin-Wiley Corp.*, 5 USPQ2d (Fed. Civ. 1998, *In re Geiger*, 2 USPQ2d 1276 (Fed. Cir. 1987), *N.V. Alczo v. El. duPont de Nemours & Co.*, 1 USPQ2d 1081 (Fed. Cir. 1987), *Orthokinetics, Inc. v. Safety Travel Chairs, Inc.*, 1 USPQ2d 1081 (Fed. Cir. 1986) and *Medtronic, Inc. v. Cardiac Pacemakers, Inc.*, 220 USPQ97 (Fed. Civ. 1983). It appears that here we have at best only a suggestion to try rather than a definite prediction that the reaction is obvious.

A number of decisions find nonobviousness and patentability because of uncertainty in the art or the absence of a reasonable probability of success. *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 231 USPQ 81 (Fed. Cir. 1986). *Ortho Pharmaceutical Corp. v. Smith*, 22 USPQ2d 1119 (Fed. Cir. 1992). *Merck & Co. v. Danbury Pharmacal Inc.*, 8 USPQ2d 1793 (D. Del. 1988). In this regard, the Federal Circuit has noted:

“Where claimed subject matter has been rejected as obvious in view of a combination of prior art references, a proper analysis under § 103 requires, inter alia, consideration of two factors: (1) whether the prior art would have suggested to those of ordinary skill in the art that they should make the claimed composition or device, or carry out the claimed process; and (2) whether the prior art would also have revealed that in so making or carrying out,

those of ordinary skill would have a reasonable expectation of success. . . Both the suggestion and the reasonable expectation of success must be founded in the prior art, not in the applicant's disclosure."

*In re Vaeck*, 20 USPQ 1442 (Fed. Cir. 1991).

Muffler states the following: "Any organic starting compound can be used for the procedure that is substituted on at least one position by nucleophilically substitutable chlorine." (emphasis added). U.S. Patent 4,874,901 to Halpern et al. (attached hereto in the Evidence Appendix) includes three examples, which are covered by these definitions. These are the following:

1.  $\text{CF}_3\text{CHClOCHF}_2 + \text{KF} \rightarrow \text{CF}_3\text{CHFOCHF}_2$
2.  $(\text{CF}_3)_2\text{CHOCHCl}_2 + \text{NaF} \rightarrow (\text{CF}_3)_2\text{CHOCHF}_2$
3.  $(\text{CF}_3)_2\text{CHOCH}_2\text{Cl} + \text{KF} \rightarrow (\text{CF}_3)_2\text{CHOCHF}_2$

In all three of these examples the chlorine is "nucleophilically" substituted it is well known that these NaF and KF reactions are nucleophilic reactions. Therefore, based on the statement in the Muffler patent, one would expect these reactions to work with hydrofluorides.

If one uses the Examiner's argument that the reaction of  $(\text{CF}_3)_2\text{CHOCHCl}_2$  is obvious then the other two reactions are also obvious. If these reactions do not proceed then the reaction is less obvious than the Examiner proposes. The chloroethers in examples 1 and 2, do not, in fact, react with amine hydrofluorides to give the expected products. Thus, there are experimental data relative to three reactions all of which should work based on the criteria outlined in the Muffler patent and the U.S. Patent. However, only one of the three does work. If two out of three reactions, which should work, do not, how can one say that the reaction is obvious?

Furthermore, in example 2, fluorination at the primary carbon off the oxygen would be expected to proceed, possibly even more readily than sevochlorane (the singly chlorinated

analogue of example 2) due to the greater nucleophilicity of the doubly chlorinated primary carbon.

Furthermore, Regan does not disclose anything considered to have a bearing on the reasons why claims 1-13 and 18-24 are believed to be nonobvious and thus patentable over Muffler. Regan describes the synthesis of sevoflurane in which  $(\text{CF}_3)_2\text{CHOCH}_2\text{Cl}$  is reacted with potassium fluoride. Regan also states that the reaction of antimony trifluoride with  $(\text{CF}_3)_2\text{CHOCH}_2\text{Cl}$  does not produce sevoflurane  $((\text{CF}_3)_2\text{CHOCH}_2\text{F})$ . Column 3, lines 1 to 10. This occurs despite the usefulness of antimony trifluoride in preparing  $(\text{CF}_3)_2\text{CHOCHF}_2$  and  $(\text{CF}_3)_2\text{CHOCHFCl}$  from the corresponding chlorinated ethers. Thus, Regan teaches the unpredictable results obtained by switching from one fluorinating agent to another.

Applicant submits that 1) the teachings of Regan (the selective behavior of antimony trifluoride) and 2) the failure of nucleophilically substitutable compounds from the examples Halpern et al. to fluorinate indicates the true state of the art with respect to the fluorination of chloroethers. It is not simply a function of nucleophilic susceptibility of the chlorine as implied by the statement from the Muffler patent quoted on page 5 herein. Instead, fluorination of chloroethers has an as yet unpredictable dependence on additional factors such as the fluorination agent used, the position of the chlorine, and other structural parameters of the chloroether substrate.

In view of the foregoing, claims 1-13 and 18-24 are believed to patentably distinguishable over Muffler in view of Regan within the meaning of 35 U.S.C. 103.

### ***Double Patenting***

Claims 1-13 and 18-24 have been rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-25 of U.S. Patent No. 5,969,193.

Serial No.: 10/644,500  
Response filed with RCE  
Reply to Office Action of January 27, 2004

Attorney Docket No.: 026403.00272

Applicant believes this ground of rejection has been obviated by virtue of the Terminal Disclaimer filed December 17, 2004, as stated the Office Communication dated March 29, 2005.


***Conclusion***

Accordingly, it is this submitted that the present claims are patentable over the cited art and are in condition for allowance which is respectfully requested.

If the Examiner has any further questions or concerns, the Examiner is invited to contact the Applicant's undersigned attorney/agent.

If any fees are occasioned by this Response, the Commissioner is hereby authorized to charge them to, or to credit, Deposit Account 08-2442 of the undersigned.

Respectfully submitted,  
HODGSON RUSS LLP  
Attorneys for Applicants

By:   
Rachel S. Watt  
Reg. No. 46,186

Date: October 2, 2006

HODGSON RUSS LLP  
One M&T Plaza  
Suite 2000  
Buffalo, New York 14203-2391  
Tel: (716) 856-4000

## EVIDENCE APPENDIX

### EXAMPLE 1

#### Reaction of $\text{CF}_3\text{CHClOCHF}_2$ with Triethyl amine Hydrofluoride

$\text{CF}_3\text{CHClOCHF}_2$  (46g, 0.25 mole) was mixed with  $(\text{Et})_3\text{N} \bullet 3\text{HF}$  (0.1 mole) and  $(\text{Et})_3\text{N}$  (0.2 mole). (Note: this is equivalent to 0.3 mole of  $(\text{Et})_3\text{N} \bullet \text{HF}$ ). There was a small exotherm observed on mixing. The resulting clear solution was refluxed for 16 hours using a water-cooled reflux condenser, the exit of which was connection to a "Dry Ice" trap in order to trap any  $\text{CF}_3\text{CFOCHF}_2$  (b.p.  $23^\circ\text{C}$ ) which might be formed. At the end of 16 hours, the reaction mixture was washed with water and dilute HCl and dried with  $\text{K}_2\text{CO}_3$ . 44g of product was recovered which was analyzed by gas chromatography using a 15' x 1/8" 20% carbowax 20m on 8100 mesh chromsorb WHP column at  $60^\circ\text{C}$ . The product was 99.92% starting ether  $\text{CF}_3\text{CHClOCHF}_2$ . There was no  $\text{CF}_3\text{CFHOCHF}_2$  collected in the "Dry Ice" trap. The fact that this ether does not react is very telling since it is structurally so closely related to one of the compounds in the Muffler patent  $\text{CF}_3\text{CHClOCH}_3$ .

### EXAMPLE 2

#### Reaction of $(\text{CF}_3)_2\text{CH-OCHCl}_2$ with Triethyl amine Hydrofluoride

$(\text{CF}_3)_2\text{CH-OCHCl}_2$  (11.7g 0.05 mole) was mixed with 3.2g  $(\text{Et})_3\text{N} \bullet 3\text{HF}$  (3.2g, 0.02 mole) and  $(\text{Et})_3\text{N}$  (4g, 0.04 mole). (This makes 0.06 mole of  $(\text{Et})_3\text{N} \bullet \text{HF}$ ) to give a clear solution with a very small amount of ppt. This solution was heated at  $60^\circ\text{C}$  for eight hours. There was no precipitate of  $(\text{Et})_3\text{N} \bullet \text{HCl}$  formed. The product was washed with water and dilute HCl and dried with  $\text{K}_2\text{CO}_3$  to give 8g of product. This product was analyzed by gas chromatography using the same conditions as in Experiment #1. This product was essentially uncharged starting material  $(\text{CF}_3)_2\text{CH-OCHCl}_2$  (95%).